Scientific Opinion on a request from the European Commission for the assessment of the new scientific elements supporting the prolongation of prohibition of the placing on the market of maize MON 863 for food and feed purposes in Austria

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Abstract: Austria notified the European Commission of its new scientific elements justifying the prolongation for three additional years of the implementation of a national safeguard measure prohibiting the placing on the market of genetically modified maize MON 863 in Austria. Subsequently, the European Commission asked the European Food Safety Authority (EFSA) to assess the new scientific information supporting the prolongation of the prohibition. Having considered the information provided by Austria and all relevant scientific publications, the EFSA Panel on Genetically Modified Organisms (GMO Panel) concluded that the new scientific elements submitted by the Austrian Authorities do not lead EFSA to reconsider the conclusions in its opinions on maize MON 863.

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SCIENTIFIC OPINION

Scientific Opinion on a request from the European Commission for the assessment of the new scientific elements supporting the prolongation of prohibition of the placing on the market of maize MON 863 for food and feed purposes in Austria[1]

EFSA Panel on Genetically Modified Organisms (GMO)[2,3]

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ABSTRACT

Austria notified the European Commission of its new scientific elements justifying the prolongation for three additional years of the implementation of a national safeguard measure prohibiting the placing on the market of genetically modified maize MON 863 in Austria. Subsequently, the European Commission asked the European Food Safety Authority (EFSA) to assess the new scientific information supporting the prolongation of the prohibition. Having considered the information provided by Austria and all relevant scientific publications, the EFSA Panel on Genetically Modified Organisms (GMO Panel) concluded that the new scientific elements submitted by the Austrian Authorities do not lead EFSA to reconsider the conclusions in its opinions on maize MON 863.

KEY WORDS

GMOs, maize (*Zea mays* L.), MON 863, safeguard clause, human and animal health, environment, Directive 2001/18/EC

[1] On request from the European Commission, Question No EFSA-Q-2013-00310, adopted on 23 October 2013.

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SUMMARY

Following a request from the European Commission (EC), the Panel on Genetically Modified Organisms (GMO Panel) was asked to deliver a scientific opinion on the new scientific information provided by Austria to support the prolongation of prohibition for the placing on the market of genetically modified (GM) maize MON 863 in Austria.

In November 2012, Austria notified the EC of its scientific elements justifying prolongation of its national safeguard measure prohibiting the placing on the market of GM maize MON 863 in Austria.

On 13 March 2013, the European Food Safety Authority (EFSA) was requested by the EC to assess the new scientific information submitted by the Austrian Authorities justifying prolongation of their national safeguard measure concerning maize MON 863.

In the light of the information provided by Austria in support of the prolongation of its safeguard clause, and having considered all relevant scientific publications, the GMO Panel concluded that the new scientific elements submitted by the Austrian Authorities do not lead EFSA to reconsider the conclusions in its opinions on maize MON 863.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

MON 863 maize is authorised in the European Union for food and feed containing, consisting of, or food produced from MON 863 (with the exception of food additives) and for other uses with the exception of cultivation. This GM maize is currently under renewal of its authorisation for the food additives and feed produced from MON 863. The renewal application received a favourable opinion from EFSA in March 2010.

In March 2009, Austria notified to the Commission the national safeguard measure on maize MON 863 accompanied by scientific argumentation. In June 2009, EFSA issued a scientific opinion concluding that there was no scientific evidence justifying the invocation of a safeguard clause under Article 23 of Directive 2001/18/EC for the marketing of maize MON 863 for its intended uses in Austria.

In November 2012, Austria notified to the Commission its Ordinance BGBI. II Nr. 319/2012 of 27 September 2012 prolonging, for three additional years, the implementation of the national safeguard measure on maize MON 863 accompanied by new scientific argumentation.

In order for the Commission to appropriately follow-up on this safeguard clause, it was deemed appropriate for EFSA to assess the new scientific elements provided by Austria to justify its decision.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

EFSA was requested in accordance with Article 29 of Regulation (EC) No 178/2002 to assess the new scientific information submitted by the Austrian Authorities justifying prolongation of their national safeguard measure concerning GM maize MON 863 and to identify whether these new scientific elements might lead the EFSA to reconsider its related opinions on GM maize MON 863.

ASSESSMENT

1. Introduction

Directive 2001/18/EC allows the Member States to invoke safeguard measures on specific genetically modified organisms (GMOs) in the case where new or additional information, made available since the date of the consent, or reassessment of existing information on the basis of new or additional scientific knowledge would affect the risk assessment of an authorised GMO. Austria seeks to provisionally prohibit the marketing of maize MON 863 in Austria.

The EFSA GMO Panel examined the set of supporting documents submitted by Austria and assessed whether the submitted documents provide new scientific information that would change the outcome of previous risk assessments and lead the GMO Panel to reconsider its opinions on GM maize MON 863 (EFSA, 2004a, 2009a).

The GMO Panel looked for evidence of GMO-specific risks, taking into consideration the EFSA GMO Panel Guidance for risk assessment of food and feed from genetically modified plants (EFSA GMO Panel, 2011) as well as previous risk assessments related to maize MON 863. In addition, the GMO Panel considered the relevance of the concerns raised by Austria in the light of the most recent scientific data and relevant peer-reviewed publications regarding the use of specific antibiotic resistance genes as marker genes in GM plants.

A meeting was held on 20 June 2013 between the Austrian delegation and EFSA staff and appointed experts. This allowed the argumentation to be presented and facilitated clarifications on issues related to the documentation provided by Austria. Following questions by the EFSA experts, Austria provided additional information on 31 July 2013 (minutes of the meeting will be published on the EFSA website).

2. Summary of concerns raised by Austria

The GMO Panel interprets the documentation provided by Austria as raising the following issues:

- the levels of *npt*II which occur naturally in Austrian isolates from human clinical samples, and in soil and feed samples, were considered by Austria to be low and a long-term exposure of these environments to plant DNA carrying *npt*II might elevate the abundance of this resistance determinant (Sections 3.1 and 3.2);
- transformation of bacteria with plant-derived DNA fragments would have the potential to result in the formation of mosaic genes (Section 3.3);
- as horizontal gene transfer events are difficult to observe, a model was constructed to simulate the spread of a novel gene in a bacterial population and the most relevant parameters were discussed (Section 3.4);
- shortcomings in the toxicological risk assessment of maize MON 863 (Section 4).

3. Frequency of environmental antibiotic resistance and the risk assessment of the *npt*II gene

3.1. Prevalence of *npt*II in human pathogen isolates

Austria reported data on the analysis of the presence of *npt*II in human clinical isolates collected in Austria. These included isolates of *Escherichia coli*, *Enterococcus faecalis*, *Enterococcus faecium*, *Pseudomonas aeruginosa* and *Staphylococcus* spp. collected during 2010 and 2011 and in *Salmonella enterica* subsp. *enterica* isolates collected during 2008–2010. A total of approximately 10 400 isolates was analysed. None of the isolates carried the *npt*II gene except for a single *Salmonella* strain. No

further information on the genetic background of resistance in this *Salmonella* strain has been provided.

Austria concluded that the prevalence of *npt*II in the human pathogenic strains collected in Austria was low and indicative of a resistance gene pool depleted of *npt*II. Austria argued that such a resistance gene pool might be "receptive for additional *npt*II gene copies from external sources". It was argued further that, although plant to bacteria gene transfer rates are extremely infrequent under naturally occurring conditions, long-term and constant exposure of bacteria to DNA containing an antibiotic resistance marker (ARM) gene would increase the contact frequency between competent bacteria and resistance gene fragments. Therefore, under certain selection conditions, there would be the potential to induce changes in the frequency of *npt*II gene copies in bacterial populations with a low endogenous *npt*II baseline. Austria also concluded that it cannot be entirely excluded that an increase in resistant bacteria would occur following an introduction of ARM genes into the accessible gene pool of the investigated bacteria.

The EFSA GMO Panel does not share the concept of a "receptive" gene pool in Austria's argumentation. The GMO Panel reiterates that the distribution of *npt*II in bacteria, even in cases where the prevalence is low, provides opportunities for transfer of this gene within bacterial communities. Transfer among bacterial community members occurs by the highly efficient method of conjugation and to a lesser extent by transduction or transformation. On the other hand, horizontal gene transfer from plant to bacterial DNA has been shown to only occur by transformation, and several factors limiting its frequency are recognised (EFSA, 2009b). Accordingly, such transfer would be much less likely to occur than that between bacteria, even in bacterial populations with a low level of *npt*II present.

Data provided by Austria show kanamycin[4] resistance in human clinical isolates. It should be stressed that, in clinical settings, the use of antibiotics is a key factor in the selection and dissemination of antibiotic resistance genes among bacteria in the immediate environment (EFSA, 2009b).

3.2. Prevalence of *npt*II in soil samples

Austria submitted data on the analysis of the prevalence of *npt*II in 100 samples of soils not exposed to GM crops. Each sample consisted of a combination of 10 single soil extractions from 50 maize and 50 potato fields. In the analysis of total DNA per soil sample, the *npt*II gene was found in 6 % of the fields (95 % confidence interval 2.2–12.6 %), with a mean number of copies in the positive samples of 340 per g of soil (range 31–856). An average of 8.29 % of all cultivable bacteria from 10 fields were resistant to kanamycin (range 0.47–19.12 %), but none of the 396 kanamycin-resistant strains isolated and characterised carried the *npt*II gene (95% confidence interval 0–0.8 %).

Austria concluded that the naturally occurring background load of *npt*II resistance genes in agricultural habitats used for the cultivation of maize and potatoes in Austria was low. Austria argued that the resistance gene pools under investigation appear not to be "saturated" but "receptive for the input of exogenous DNA carrying aminoglycoside phosphotransferase (3′)-IIa gene homologues". The Austrian Authorities consider that a long-term and constant exposure of these habitats to exogenous DNA carrying *npt*II via root exudates, or following plant decay, might be capable of elevating the abundance of this resistance determinant in relevant environments.

[4] Kanamycin and neomycin have been recategorised by the WHO from 'Highly Important Antimicrobial' to 'Critically Important Antimicrobial' (WHO, 2012). The GMO Panel reiterates its view that, while some knowledge gaps remain regarding the understanding of the natural reservoir of antibiotic resistance genes and their role in natural bacterial communities not exposed to industrially produced antibiotics, the key role of selection by antibiotic usage in the development of resistance is indisputable (EFSA, 2009b). Therefore, the WHO recategorisation may impact the development of bacterial resistance via antibiotic selection pressure (because of change of use) but has no impact on the barriers limiting the transfer frequency of *npt*II from plant to bacterial DNA, which remains several orders of magnitude lower than the transfer rates between bacteria.

The EFSA GMO Panel does not share the concept of "saturated" and "receptive" in Austria's argumentation. Data provided by Austria show the presence of *npt*II in the soil samples analysed. In any case, the GMO Panel notes that maize MON 863 is not authorised for cultivation in the European Union. Therefore, exposure of soil bacteria to DNA containing *npt*II from maize MON 863 released from imported plant material is expected to be very low and not relevant for soil bacterial populations.

3.3. Prevalence of *npt*II in feed samples

Austria reported results from the analysis of the presence of *npt*II in feed-associated bacteria by testing total DNA extracts of dried maize kernels and potato juice (42 samples of each). None of the DNA extracts yielded a positive result after PCR targeting the *npt*II gene. Bacterial populations associated with the maize and potato samples were cultured in kanamycin-containing medium and resistant strains were isolated and tested for the presence of *npt*II. One strain out of 167 isolates carried the *npt*II gene. The frequency of the kanamycin resistance phenotype varied considerably, from 0.01 % to 73.05 % in maize samples and from 0.002 % to 6.6 % in potato samples. Austria concluded that, although only a small number of bacterial samples were tested, the results support the hypothesis that *npt*II occurrence is low in maize and potatoes cultivated and used as feed in Austria.

The EFSA GMO Panel reiterates that the distribution of *npt*II in naturally occurring bacteria provides opportunities for transfer of this gene between bacteria by the highly efficient method of conjugation and to a lesser extent by transduction or transformation. Horizontal gene transfer from plant to bacteria can occur only by transformation, and several factors limiting its frequency are recognised (EFSA, 2009b). The EFSA GMO Panel therefore stresses that transfer of the *npt*II gene from plant to bacteria would be expected to occur with a frequency several orders of magnitude lower than that between bacteria (EFSA, 2009b).

3.4. Mosaic genes

Austria reported results from bioinformatic analyses, which showed no extended regions of DNA similarity between *npt*II gene sequences and other aminoglycoside phosphotransferase genes. The contiguous stretches of identical sequences were short. Austria concluded that homologous recombination between *npt*II and other aminoglycoside phosphotransferase genes would not be the primary route for the exchange of DNA fragments and sequence evolution.

Austria further investigated the possibility for exchange of DNA sequences between aminoglycoside phosphotransferase genes by illegitimate recombination on the basis of regions with microhomologies. Sequence alignments using standard parameters of the BLAST algorithm did not reveal the presence of *npt*II mosaic genes of natural origin in GenBank sequence entries. Data retrieved from bioinformatic analysis did not support the hypothesis of an involvement of the *npt*II gene in the formation of mosaic genes with altered resistance patterns within the family of aminoglycoside phosphotransferases.

Austria also investigated, experimentally, the potential for *npt*II to generate mosaic genes with related phosphotransferase genes. In a first step, the natural *aph(3″)-Ib* or *aph(3′)-Va* gene was introduced into the genome of *Acinetobacter baylyi* bacterium. Subsequently, these strains containing either the *aph(3″)-Ib* or the *aph(3′)-Va* gene were transformed with linearised plasmids containing *npt*II flanked on one side by a stretch of DNA (anchor) homologous to *Acinetobacter baylyi* genomic DNA flanking the genes introduced in the first step, thus potentially facilitating homologous recombination. No transformants were obtained with the *Acinetobacter baylyi* containing the *aph(3″)-Ib* sequence. Transformation of *Acinetobacter baylyi* containing the *aph(3′)-Va* sequence yielded colonies with decreased susceptibility to kanamycin as analysed by a disc diffusion test. Austria argued that "recombination has likely occurred between the two genes, as it would be the case with the formation of mosaic genes". Austria concluded that the phenotypic data obtained indicated the induction of an increase in resistance to kanamycin after uptake of *npt*II, involving formation of mosaic structures. No sequencing data were provided to support this interpretation.

The EFSA GMO Panel agrees with Austria that no mosaic structures of aminoglycoside phosphotransferase genes have been reported in bacteria although these genes are widespread in many environments. The formation of mosaic structures from the transfer of the *npt*II gene from plant to bacteria would be expected to occur with a frequency several orders of magnitude lower than the frequency obtained by transfer of DNA between bacteria. The GMO Panel concludes that the data provided do not indicate the existence of mosaic structures of aminoglycoside phosphotransferase genes and no new hazard has been identified.

The GMO Panel considers that Austria's interpretation of the experimental results of decreased susceptibility to kanamycin as a result of the formation of a mosaic gene is premature, and that verification would need, as a minimum requirement, the sequence analysis of the colonies with reduced susceptibility to the antibiotic.

3.5. Antibiotic selection pressure and model for horizontal gene transfer

Since horizontal gene transfers are rare events and thus difficult to observe, Austria constructed a model simulating the horizontal transfer of plant-derived antibiotic resistance genes into soil bacterial communities, on the basis of results from Townsend et al. (2012). One aim of this modelling exercise was to determine which parameters have the largest influence on the outcome. Austria concluded that fixation of a new trait is mostly dependent on the selection pressure prevailing in the relevant habitat. The frequency of horizontal gene transfer (transfer rate) and the population size also play a (smaller) role concerning the fixation of a new trait in a population.

The GMO Panel reiterates that maize MON 863 is not authorised for cultivation in the European Union. Therefore, exposure of soil bacteria to DNA containing *npt*II from maize MON 863 is expected to be very low. The GMO Panel is of the opinion that the exposure levels considered in the model are unrealistically high even in the case of cultivation of the GM maize.

The Panel agrees with Austria that antibiotic selection pressure is a key factor in the selection and dissemination of antibiotic resistance genes in bacterial populations. Even if bacteria containing *npt*II are present at a low level in the bacterial gene pool, the transfer rate of *npt*II between bacteria would occur at a frequency several orders of magnitude greater than the rate calculated in laboratory conditions for a transfer of plant DNA to bacteria.

4. Toxicological risk assessment

The GMO Panel notes that in the concerns detailed below by Austria no new scientific data have been provided to support Austria's claims and no new hazards have been identified.

4.1. Issues related specifically to maize MON 863

Concern of Austria: The 90-day toxicity study in rats is based on an OECD test design outdated at the time of planning and realisation of the study (thus, certain neuro-/immunotoxic endpoints being already state-of-the-art were not investigated).

> The basic requirements according to OECD Guideline 408 have not changed in the intervening nine years since the study was reported in 2004. Neurological and immunological endpoints are not considered part of the standard battery of observations; they are considered optional and triggered by other indications. Since such indications did not exist in the case of MON863, the GMO Panel did not consider it necessary to investigate these endpoints.

Concern of Austria: Significant differences are not classified as biologically relevant (arguments: within statistical bandwidth, no dose-related effects, no effects in both sexes, etc.) Further tests to investigate potential adverse effects were not carried out (long term studies, developmental/reproductive toxicity studies).

Each individual endpoint showing significant differences was described and assessed for its biological relevance, as documented in the Scientific Opinion of the EFSA GMO Panel (EFSA, 2004a). A re-analysis of the data carried out in 2007 came to the same conclusion as the previous assessment (EFSA, 2007a, b).

Concern of Austria: No rationale is given whether 33 % is indeed the highest possible level for maize in the diet of rats (accordingly, higher dosages may have been used).

The applicant, in its notification C/DE/02/9, submitted within the framework of Directive 2001/18/EC and Regulation 258/97, calculated the mean and 97.5th percentile of maize consumption (g/kg body weight per day) in Europe based on UK data (the Nutritional Survey of British Adults and the UK National Diet) and found that it is of the same order as the doses used in the animal experiment.

4.2. General issues raised

Concern of Austria: Studies in broiler chicken are mainly designed to investigate efficacy and tolerance and cannot be a substitute for lege artis toxicity studies.

The GMO Panel agrees with this statement and does not require such studies in its toxicological assessment. However, such studies can show differences in endpoints such as growth rate, morbidity and mortality between animals fed the GM diet and those fed a conventional counterpart diet, which are of relevance to the safety assessment.

Concern of Austria: Intravenous administration of the trans-proteins does not reflect the natural route of exposure.

The GMO Panel agrees with this comment. It is noted that the comment is not relevant since in the context of the most recent application on maize MON 863 (EFSA GMO Panel, 2010) no studies with intravenous administration of the newly expressed proteins were provided.

Concern of Austria: There are some deficits that become apparent in studies performed by the applicant and cited by Hammond et al. (2006).

– The study design provided a majority of reference groups (60–80 %), and thus the data of the verum group were potentially masked by comparing to broad ranges in their statistical relevance.

The EFSA GMO Panel has addressed this point in its statements (EFSA, 2004b, 2007b): in the event that statistically relevant changes in biological parameters have been identified, their natural variations must be taken into account in order to assess the biological relevance. To this end the use of animals of the same strain and age, fed with diets containing other commercial maize varieties, is most relevant.

– Rules of good practice require examination of histo-pathological endpoints. However, these requirements were not fully met.

The statement is not clear. Histo-pathological endpoints, examined by the applicant, have been assessed by the EFSA GMO Panel (EFSA, 2004a, b, 2007a, b).

– Significant differences which had been observed were downgraded using arguments such as "no dose-related trends", "within historical control", and "pathologically irrelevant".

The concept that, while statistics provide a tool to compare treated groups to controls, the assessment of the biological importance of any "statistically significant" effect requires a broader evaluation of the data is the accepted practice in the toxicological assessment (Wilson et al., 2001).

CONCLUSIONS

The EFSA GMO Panel concluded that the new scientific elements presented in the data package submitted by the Austrian Authorities do not lead EFSA to reconsider the conclusions in its opinions on maize MON 863.

DOCUMENTATION PROVIDED TO EFSA

1. Letter, received 13 March 2013, with supporting documents from Ladislav Miko, Deputy Director-General for the food chain EC, to Catherine Geslain-Lanéelle, Executive Director EFSA (ref. Ares(2013)327179), requesting the assessment by EFSA of the new scientific elements provided by Austria in support of its decision to prolong its national safeguard measure under Article 23 of Directive 2001/18/EC for GM maize MON 863 and comprising the following supporting documents:

   – Frequency of environmental antibiotic resistance, baseline prevalence of neomycin phosphotransferase genes II and III in maize and potato fields, feed and human bacterial pathogens in Austria

      - Executive summary
      - part A: *npt*II and *npt*III prevalence in human pathogens
      - part B: *npt*II and *npt*III prevalence in soil
      - part C: *npt*II and *npt*III prevalence in feed
      - part D: mosaic genes, selection pressure, modelling horizontal gene transfer in soil habitats;
      - part E: PCR detection methods;

   – AGES Englische Fassung/Verlängerung ImportverboteMais MON863, Raps Ms8xRf3, Raps GT73

REFERENCES

EFSA (European Food Safety Authority), 2004a. Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the Notification (Reference C/DE/02/9) for the placing on the market of insect protected genetically modified maize MON863 and MON863xMON810, for import and processing, under Part C of Directive 2001/18/EC from Monsanto. The EFSA Journal 2004, 49, 1-25. doi:10.2903/j.efsa.2004.49 Available online: http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178620772339.htm

EFSA (European Food Safety Authority), 2004b. Statement of the Scientific Panel on Genetically Modified Organisms on an evaluation of the 13-week rat feeding study on MON 863 maize, submitted by the German authorities to the European Commission. The EFSA Journal, 2004, 750, 1-5. Available online: http://www.efsa.europa.eu/en/efsajournal/pub/750.htm

EFSA (European Food Safety Authority), 2007a. EFSA review of statistical analyses conducted for the assessment of the MON 863 90-day rat feeding study. The EFSA Journal 2007, 19r, 1-146. doi:10.2903/j.efsa.2007.19r Available online: http://www.efsa.europa.eu/en/efsajournal/pub/19r.htm

EFSA (European Food Safety Authority), 2007b. Statement on the analysis of data from a 90-day rat feeding study with MON 863 maize by the Scientific Panel on genetically modified organisms (GMO). The EFSA Journal 2007, 753, 1-5. doi:10.2903/j.efsa.2007.753 Available online: http://www.efsa.europa.eu/en/efsajournal/pub/753.htm

EFSA (European Food Safety Authority), 2009a. Scientific Opinion of the Panel on Genetically Modified Organisms on a request from the European Commission related to the safeguard clause invoked by Austria on maize lines MON 863 according to Article 23 of Directive 2001/18/EC. The EFSA Journal 2009, 1152, 1-18. doi:10.2903/j.efsa.2009.1152

EFSA (European Food Safety Authority), 2009b. Statement of EFSA on the consolidated presentation of the joint Scientific Opinion of the GMO and BIOHAZ Panels on the "Use of Antibiotic Resistance Genes as Marker Genes in Genetically Modified Plants" and the Scientific Opinion of the GMO Panel on "Consequences of the Opinion on the Use of Antibiotic Resistance Genes as Marker Genes in Genetically Modified Plants on Previous EFSA Assessments of Individual GM Plants". The EFSA Journal 2009, 1108, 1-8. doi:10.2903/j.efsa.2009.1108

EFSA Panel on Genetically Modified Organisms (GMO), 2010. Scientific Opinion on application (EFSA-GMO-RX-MON863[8.1.b/20.1.b]) for renewal of the authorisation for continued marketing of existing feed materials, feed additives and food additives produced from maize MON863 under Regulation (EC) No 1829/2003 from Monsanto. EFSA Journal 2010;8(3):1562, 15 pp. doi:10.2903/j.efsa.2010.1562

EFSA Panel on Genetically Modified Organisms (GMO), 2011. Guidance for risk assessment of food and feed from genetically modified plants. EFSA Journal 2011;9(5):2150, 37 pp. doi:10.2903/j.efsa.2011.2150

Townsend JP, Bøhn T and Nielsen KM, 2012. Assessing the probability of detection of horizontal gene transfer events in bacterial populations. Frontiers in Microbiology, 3, 27. doi: 10.3389/fmicb.2012.00027

WHO (World Health Organisation), 2012. Critically important antimicrobials for human medicine, 3rd revision 2011. WHO Press, World Health Organisation, Geneva, 31 pp.

Wilson NH, Hardisty JF and Hayes JR, 2001. Short-term, subchronic, and chronic toxicology studies. In: Principles and methods of toxicology, 4th edition. Ed. Hayes AW. Taylor & Francis, Philadelphia, PA, USA, 917-957.